

New claims 51-54 and 55-58 are directed to the methods of claims 23 and 37, respectively, utilizing specific bacteriophage compositions. Support for claims 51, 52, 55, and 56 can be found in the specification at, for example, col. 15, lines 36-59 (“Two particularly virulent preparations were selected on the basis of concentration and isolate sensitivity. . . Samples of virulent bacteriophage 146A and 173A preparations were deposited in the ATCC, 12301 Parklawn Drive, Rockville, Md., 20852 on Apr. 15, 1997 and accorded ATCC accession Nos. 55950 and 55951, respectively.”) Support for claims 53, 54, 57, and 58 can be found in the specification at, for example, col. 16, lines 6-14 (“A sample of virulent bacteriophage 262A preparation was deposited in the ATCC at the above address, on Apr. 15, 1997 and accorded ATCC accession No. 55955. . . . A sample of virulent bacteriophage 174A preparation was deposited in the ATCC at the above address on Apr. 15, 1997 and accorded ATCC accession No. 55956.”)

As the forgoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

## **II. Rejections under 35 U.S.C. § 102**

### **A. Merril, U.S. Patent No. 5,688,501**

In the Advisory Action mailed on October 22, 2002, the Examiner maintained the previous rejection of claims 23-25, 29-30, 33-39, 43-44, and 47-50 under 35 USC §102(e) as being allegedly anticipated by Merrill et al. (“Merril”), U.S. Patent Number 5,688,501. Applicants respectfully traverse this ground for rejection.

#### **1. Merril Does not Teach Virulent Bacteriophage Having a Broad Host Range**

The Examiner alleged that Merrill discloses a lambda phage composition having a wide host range. In contrast to the Examiner’s assertion, Merrill does not teach Applicants’ claimed invention, directed to methods utilizing a purified, host-specific, non-toxic, wide host range, and virulent bacteriophage preparation.

Merrill itself does not teach a bacteriophage preparation having a wide host range. In fact, Merrill teaches a bacteriophage preparation that is specific for a particular bacterial strain. Specifically, Merrill teach that the bacteriophage “are specific for each of the bacterial strain

of interest.” *See* column 6, lines 63-67. Furthermore, Merrill teaches “a full array of anti-HPS selected and/or anti-HDS engineered bacteriophage is developed for virtually all the bacterial (and other applicable) pathogens.” *See* column 6, line 67, through column 7, line 5.

In contrast, the claimed invention recites methods utilizing bacteriophage which have a broad host range. Merrill require “a full array” of bacteriophage for treatment, while Applicants’ claimed methods utilize bacteriophage that enable treatment with a single bacteriophage preparation. Accordingly, as Merrill does not describe all of the elements required by Applicants’ claims, the claimed invention is not anticipated by Merrill. Applicants respectfully request withdrawal of the rejections.

**2. Merril Does not Teach a Virulent Bacteriophage Preparation Selected Based on the Ability to Kill Bacteria**

Merril does not anticipate the claimed invention as the reference does not teach methods of utilizing a virulent bacteriophage selected based on ability to kill bacteria.

Merril teaches a method for producing bacteriophage that have increased resistance to inactivation by the treated animal’s host defense system. Specifically, Merrill disclose bacteriophages, developed by serial passage or genetic engineering, that remain in the host’s body for longer periods of time compared with the wild-type phage. In addition, Merrill teaches an anti-HDS modified bacteriophage with “a half-life 15 % greater than the half-life of the original wild-type phage from which it was derived.” *See* column 5, lines 10-12. Finally, Merrill teaches that: “[a] 15 % longer half-life indicates a successful delay of inactivation by the HDS.” *See* column 5, lines 17-19.

In view of Merrill’s objective of producing bacteriophage with prolonged half-lives, Merrill discloses methods for mutagenizing the phage to produce bacteriophage that have a longer survival time in a host, compared with a wild-type phage. *See* column 5, lines 38-45. Additionally, Merrill teaches genetically engineering a phage “to express molecules on its surface coat, where said molecules antagonize, inactivate, or in some other manner impeded those actions of the HDS that would otherwise reduce the viability of the administered

phages. See column 5, lines 50-57. Clearly, the inventive methods of Merrill are directed to the isolation of bacteriophage that are able to survive longer in the host body.

Bacteriophage having a prolonged circulation time and viability do not preclude the bacteriophage from being *less* virulent and therefore *ineffective* as a treatment. Furthermore, the teachings of Merrill fail to establish bacteriophage with increased capabilities of killing bacteria. Therefore, the teachings of Merrill do not anticipate the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections.

**B. Norris, U.S. Patent No. 4,957,686**

The Examiner maintained the previous rejection of claims 23-24, 33-34, 37-38, and 47-48 under 35 U.S.C. § 102(b) as being allegedly anticipated by Norris., U.S. Patent Number 4,957,686. Applicants respectfully traverse this ground for rejection.

The Examiner alleged that the bacteriophage preparation of Norris has a wide host range. In contrast to the Examiner's assertion, Norris does not teach Applicants' claimed invention, directed to methods of utilizing a purified, host-specific, non-toxic, wide host range, and virulent bacteriophage preparation.

Norris fails to teach a bacteriophage preparation with a wide-host range. Specifically, Norris teaches that: "[e]ach phage is specific to one kind of bacteria and does not attack other cells, bacteria, or other." See column 3, lines 28-30. Furthermore, Norris teaches that the "phages contact other bacteria of the kind to which they are specific and destroy these...." See column 3, lines 36-40. Accordingly, because the claimed invention is not anticipated by Norris, withdrawal of the rejection is courteously requested.

### **III. Rejections under 35 U.S.C. § 103**

#### **A. Rejection Over Merrill in View of Denney**

Claims 26 and 40 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Merrill in view of Denney (U.S. Patent No. 3,793,151). Applicants respectfully traverse this ground for rejection.

Merrill is deficient for the reasons as discussed above. The Examiner does not rely upon Denney to remedy these deficiencies. As a *prima facie* case of obviousness requires the combination of references to teach or suggest every aspect of the claimed invention (*see* MPEP 2143.03), the combination of cited references does not render the claimed invention obvious. Accordingly, Applicants respectfully request withdrawal of the rejection.

#### **B. Rejection Over Merrill in View of He**

Claims 27 and 41 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Merrill in view of He (1992). Applicants respectfully traverse this ground for rejection.

Merrill is deficient for the reasons discussed above. The Examiner does not rely upon He to remedy these deficiencies. The combination of cited references therefore does not render the claimed invention obvious. Accordingly, Applicants respectfully request withdrawal of the rejection.

#### **C. Rejection Over Merrill in View of Sekaninova et al.**

Claims 28 and 42 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Merrill in view of Sekaninova et al. (1995). Applicants respectfully traverse this ground for rejection.

Merrill is deficient for the reasons discussed above. The Examiner does not rely upon Sekaninova et al. to remedy these deficiencies. The combination of references therefore does not render the claimed invention obvious. Accordingly, Applicants respectfully request withdrawal of the rejection.

**D. Rejection Over Merrill in View of Bar-Shalom et al.**

Claims 31 and 45 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Merrill in view of Bar-Shalom et al. (the '808 patent). Applicants respectfully traverse this ground for rejection.

Merrill is deficient for the reasons discussed above. The Examiner does not rely upon Bar-Shalom et al. to remedy these deficiencies. The combination of references therefore does not render the claimed invention obvious. Accordingly, Applicants respectfully request withdrawal of the rejection.

**D. Rejection Over Merrill in View of Bar-Shalom et al.**

Claim 45 was rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Merrill in view of Tomalia et al. (the '166 patent). Applicants respectfully traverse this ground for rejection.

Merrill is deficient for the reasons discussed above. The Examiner does not rely upon Tomalia et al. to remedy these deficiencies. The combination of references therefore does not render the claimed invention obvious. Accordingly, Applicants respectfully request withdrawal of the rejection.

**CONCLUSION**

In view of the foregoing arguments, the claimed invention is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

If there are any fees due in connection with the filing of this Amendment, please charge the fees to our Deposit Account No. 19-0741. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date

April 4, 2003

By

Michele M. Simkin

FOLEY & LARDNER

Washington Harbour

3000 K Street, N.W., Suite 500

Washington, D.C. 20007-5143

Telephone: (202) 672-5538

Facsimile: (202) 672-5399

Michele M. Simkin

Attorney for Applicant

Registration No. 34,717